IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s):	Turner, Jr. *et al.*	Group Art Unit:	1647
Application No.:	09/689,911	Examiner:	B. Bunner
Filed:	10/11/2000	Atty. Docket No.:	LEX-0068-USA

Title: Polynucleotides Encoding Human Galanin Family Proteins (As Amended)

AMENDMENT AND RESPONSE TO OFFICE ACTION DATED APRIL 1, 2002

Assistant Commissioner for Patents
Arlington, VA 22202

Sir:

The Applicants acknowledge the receipt of the Office Action ("the Action") mailed on April 1, 2002 (Paper No. 10), which has been carefully reviewed and studied. The Examiner is respectfully requested to enter the following amendments. Reexamination and reconsideration of the application is requested in view of the following amendments and remarks. In order to facilitate the Examiner's evaluation of the application, Applicants have attempted to address the objections and rejections in Paper No. 10 in the same order in which they were originally raised.

The Action was received by Applicants with two face pages - one dated March 11, 2002, and a second dated April 1, 2002. Based on a voice mail message received by Applicants' representative Ms. Drenda Thomas from Supervisory Examiner Kunz on April 8, 2002, the Action was remailed to Applicants on April 1, 2002, and thus the April 1, 2002 date was to be used to calculate the deadline for filing the present response. Thus, the present response is due on July 1, 2002. The response is thus timely filed. Applicants believe no fees are due in connection with this response. However, the Commissioner is authorized to charge any required fees or credit any overpayment to Deposit Account No. 50-0892.

AMENDMENT

In the specification:

Please delete the present title and replace with the new title –Polynucleotides Encoding Human Galanin Family Proteins–.

In the claims:

Please amend the claims so that the text of the amended claims read as follows:

a1

1. (Amended) An isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 1.

2. (Amended) An isolated nucleic acid molecule comprising a nucleotide sequence that:

(a) encodes the amino acid sequence shown in SEQ ID NO: 2; and

(b) hybridizes under highly stringent conditions to the nucleotide sequence of SEQ ID NO: 1 or the complement thereof.

a2

4. (Amended) An isolated nucleic acid molecule comprising a nucleotide sequence that encodes the amino acid sequence from amino acid number 33 to amino acid number 141 of SEQ ID NO:2.

Please add new claims 5-8 as follows:

a3

--5. (New) A recombinant expression vector comprising the nucleic acid molecule of claim 4.

6. (New) The recombinant expression vector of claim 5, wherein the nucleic acid molecule comprises a nucleotide sequence that encodes the amino acid sequence shown in SEQ ID NO: 2.

7. (New) The recombinant expression vector of claim 6, wherein the nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:1.

a3 cont'd 8. (New) A host cell comprising the recombinant expression vector of claim 5.--

RESPONSE

I. Status of the Claims

No claims have been canceled. Claims 1, 2 and 4 have been amended. New claims 5-8 have been added.

Claims 1-8 are therefore presently pending in the case. For the convenience of the Examiner, a clean copy of the pending claims is attached hereto as **Exhibit A**. In compliance with 37 C.F.R. § 1.121(c)(1)(ii), a marked up copy of the original claims is attached hereto as **Exhibit B**.

II. Support for the Amendments and Newly Added Claims

The specification has been amended to include a new title that is more descriptive of the invention to which the claims are directed. Support for the new title can be found in the original title, and throughout the specification and claims as originally filed. In compliance with 37 C.F.R. § 1.121(b)(1)(iii), a marked up copy of the original title is attached hereto as **Exhibit C**.

Claim 1 has been amended to further clarify the claim, and to recite that the isolated nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:1. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least in claim 1 as originally filed and in Section 5.1.

Claim 2 has been amended to recite that the stringent hybridization conditions are highly stringent hybridization conditions. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least from page 3, line 32 through page 4, line 5.

Claim 4 has been amended to recite that the isolated nucleic acid molecule comprises a nucleotide sequence that encodes the amino acid sequence from amino acid number 33 to amino acid number 141 of SEQ ID NO:2. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least in original claim 4, and at page 12, lines 8-17.

Claims 5-7 have been added to specifically recite recombinant expression vectors comprising

the isolated nucleic acid molecules of claims 4, 3 and 1, respectively. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least at page 9, lines 30-36.

Claim 8 has been added to specifically recite host cells comprising the recombinant expression vectors of claim 5. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least from page 9, line 36 to page 10, line 5.

It will be understood that no new matter is included within the new title, or the amended or newly added claims.

III. Oath/Declaration

The Action notes that the declaration is defective because non-initialed and/or non-dated alterations were made. Applicants submit herewith a supplemental declaration in compliance with 37 C.F.R. § 1.67(a), which identifies the application by application number and filing date.

IV. Objections

The Action first objects to the reference of patent applications in the disclosure, specifically those at page 12, line 23, and requests that the status of the applications be updated. Applicants can find no further information concerning these patent applications on the USPTO web site, and thus assume that the information provided in the specification is the most up-to-date information available.

The Action next objects to the title of the application as being non-descriptive. Applicants have amended the title of the present application to more accurately reflect the currently pending claims.

Applicants request that, since the objections have been overcome, these objections be withdrawn.

V. Rejection of Claims 1-4 Under 35 U.S.C. § 101

The Action first rejects claims 1-4 under 35 U.S.C. § 101, as allegedly lacking a patentable utility. Applicants respectfully traverse.

As set forth by the Federal Circuit, "(t)he threshold of utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip Inc. v. Orange*

Bang Inc., 51 USPQ2d 1700 (Fed. Cir. 1999) (citing *Brenner v. Manson*, 383 U.S. 519, 534 (1966)). Additionally, the Federal Circuit has stated that "(t)o violate § 101 the claimed device must be totally incapable of achieving a useful result." *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571 (Fed. Cir. 1992), emphasis added. *Cross v. Iizuka* (224 USPQ 739 (Fed. Cir. 1985); "*Cross*") states "any utility of the claimed compounds is sufficient to satisfy 35 U.S.C. § 101". *Cross* at 748, emphasis added. Indeed, the Federal Circuit recently emphatically confirmed that "anything under the sun that is made by man" is patentable *(State Street Bank & Trust Co. v. Signature Financial Group Inc.*, 47 USPQ2d 1596, 1600 (Fed. Cir. 1998), citing the U.S. Supreme Court's decision in *Diamond vs. Chakrabarty*, 206 USPQ 193 (S.Ct. 1980)).

In *In re Brana,* (34 USPQ2d 1436 (Fed. Cir. 1995), "*Brana*"), the Federal Circuit admonished the P.T.O. for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". *Brana* at 1442. The Federal Circuit went on to state:

> At issue in this case is an important question of the legal constraints on patent office examination practice and policy. The question is, with regard to pharmaceutical inventions, what must the applicant provide regarding the practical utility or usefulness of the invention for which patent protection is sought. This is not a new issue; it is one which we would have thought had been settled by case law years ago.

Brana at 1439, emphasis added. The choice of the phrase "utility or usefulness" in the foregoing quotation is highly pertinent. The Federal Circuit is evidently using "utility" to refer to rejections under 35 U.S.C. § 101, and is using "usefulness" to refer to rejections under 35 U.S.C. § 112, first paragraph. This is made evident in the continuing text in *Brana*, which explains the correlation between 35 U.S.C. §§ 101 and 112, first paragraph. The Federal Circuit concluded:

> FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

Brana at 1442-1443, citations omitted. The Examiner implies that a "real-world" utility does not

require "further research" (Action at page 4). However, even if, *arguendo*, further research might be required in certain aspects of the present invention, this does not preclude a finding that the invention has utility, as set forth by the Federal Circuit's holding in *Brana*, which clearly states, as highlighted in the quote above, that "pharmaceutical inventions, necessarily includes the expectation of <u>further research and development</u>" (*Brana* at 1442-1443, emphasis added). In assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is "undue", not "experimentation". *In re Angstadt and Griffin*, 190 USPQ 214 (CCPA 1976). The need for some experimentation does not render the claimed invention unpatentable. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra*; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir. 1988).

The Action next states that the invention lacks utility because the disclosure "does not disclose any working examples" (Action at page 4). This argument must fail, because it has long been established that "there is no statutory requirement for the disclosure of a specific example". *In re Gay*, 135 USPQ 311 (CCPA 1962).

The present invention has a number of substantial and credible utilities, not the least of which is in expanding the utility of data coming from the human genome project. Persons of skill in the art, as well as thousands of venture capitalists and investors, readily recognize the utility, both scientific and commercial, of genomic data in general, and specifically human genomic data. All current therapeutics used in humans directly or indirectly interact with biological sequences encoded by the human genome, and virtually all future human therapeutics shall do likewise. Consequently, billions of dollars have been invested in the human genome project, resulting in useful genomic data (see, *e.g.*, Venter *et al.*, 2001, Science *291*:1304). The results have been a stunning success, as the utility of human genomic data has been widely recognized as a great gift to humanity (see, *e.g.*, Jasny and Kennedy, 2001, Science *291*:1153). Clearly, the usefulness of human genomic data, such as the presently claimed nucleic acid molecules, is <u>substantial</u> and <u>credible</u> (worthy of billions of dollars and the creation of numerous companies focused on such information) and <u>well-established</u> (the utility of human genomic information has been clearly understood for many years).

As an additional example of the utility of the present nucleotide sequences, the specification details on page 5, lines 2-4, that the present nucleotide sequences have utility in assessing gene expression patterns using high-throughput DNA chips. Such "DNA chips" clearly have utility, as evidenced by hundreds of issued U.S. Patents, as exemplified by U.S. Patent Nos. 5,445,934, 5,556,752, 5,744,305, 5,837,832, 6,156,501 and 6,261,776. The present nucleotide sequences are clearly related to human galanins, as detailed throughout the specification. The specification also teaches that galanins are associated with a wide variety of cellular functions, including being upregulated after spinal injury and in response to estrogen, the release of growth hormone, the inhibition of insulin and somatostatin release, smooth muscle contraction and adrenal secretion (specification at page 1, lines 22-29). Therefore, as the present sequences are specific markers of the human genome, and such specific markers are targets for the discovery of drugs that are associated with human diseases and conditions associated with galanins, such as misregulated body weight, behavior modulation, pain, inflammation, neuronal repair, Alzheimer's dementia, inflammatory bowel disorders and infectious disease (specification at page 1, lines 32-36), those of skill in the art would instantly recognize that the present nucleotide sequences would be an ideal, novel candidate for assessing gene expression using such DNA chips. Clearly, compositions that enhance the utility of such DNA chips, such as the presently claimed nucleotide sequences, must in themselves be useful.

Although Applicants need only make one credible assertion of utility to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), as a further example of the utility of the presently claimed polynucleotide, the present nucleotide sequence has a specific utility in mapping the protein encoding regions of the corresponding human chromosome. Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of the human chromosome containing the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequences. In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily

appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence.

Finally, the requirements set forth in the Action for compliance with 35 U.S.C. § 101 do not comply with the requirements set forth by the Patent and Trademark Office ("the PTO") itself for compliance with 35 U.S.C. § 101. The PTO has issued numerous patents on polynucleotide sequences that have not been directly shown to be associated with the function of the protein that is set forth in the specification, or a direct association between the claimed sequences and a particular disease or condition (Action at page 6), the conditions apparently set forth by the Examiner as allegedly necessary to comply with 35 U.S.C. § 101. The Examiner is invited to review U.S. Patent Nos. 5,817,479, 5,654,173, and 5,552,2812 (each of which claims short polynucleotide fragments), and recently issued U.S. Patent No. 6,340,583 (which includes no working examples). None of these issued U.S. Patents contain examples of the "real-world" utilities that the Examiner seems to be requiring in the present Action. As issued U.S. Patents are presumed to meet all of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph (see Section VI below), Applicants submit that the presently claimed polynucleotide must also meet the requirements of 35 U.S.C. § 101.

For each of the foregoing reasons, Applicants submit that as the presently claimed nucleic acid molecules have been shown to have a substantial, specific, credible and well-established utility, the rejection of claims 1-4 under 35 U.S.C. § 101 has been overcome, and request that the rejection be withdrawn.

VI. Rejection of Claims 1 and 4 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claims 1 and 4 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by a specific, substantial, and credible utility or a well-established utility. Applicants respectfully traverse.

Applicants submit that as claims 1-4 have been shown to have "a specific, substantial, and credible utility", as detailed in section V above, the present rejection of claims 1 and 4 under 35 U.S.C. § 112, first paragraph, cannot stand.

Applicants therefore request that the rejection of claims 1 and 4 under 35 U.S.C. § 112, first

paragraph, be withdrawn.

VII. Rejection of Claims 1 and 4 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claims 1 and 4 under 35 U.S.C. § 112, first paragraph, as allegedly not providing enablement for the full scope of the claimed invention comprising a genus of at least 24 contiguous nucleotides of SEQ ID NO:1 or at least 29 amino acids from SEQ ID NO:2. While Applicants in no way agree that the present application does not provide enablement for nucleotide sequences comprising at least 24 contiguous nucleotides from SEQ ID NO:1, or 29 amino acids from SEQ ID NO:2, as claim 1 currently recites only nucleic acid molecules comprising the nucleotide sequence of SEQ ID NO:1, which is clearly enabled, and as claim 4 currently recites only nucleic acid molecules comprising a nucleotide sequence that encodes the amino acid sequence from amino acid number 33 to amino acid number 141 of SEQ ID NO:2, which is clearly enabled in the specification (see, at least, Section 5.1), the present rejection of claims 1 and 4 under 35 U.S.C. § 112, first paragraph, has been rendered moot or overcome. Applicants therefore respectfully request that the rejection of claims 1 and 4 under 35 U.S.C. § 112, first paragraph, be withdrawn.

VIII. Rejection of Claims 1 and 4 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claims 1 and 4 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Again, while Applicants in no way agree that the present application does not provide sufficient written description for nucleotide sequences comprising at least 24 contiguous nucleotides from SEQ ID NO:1, as claim 1 currently recites only nucleic acid molecules comprising the nucleotide sequence of SEQ ID NO:1, which the Action admits is disclosed in the specification (Action at page 7), the present rejection of claim 1 under 35 U.S.C. § 112, first paragraph, has been rendered moot. Furthermore, while Applicants in no way agree that the present application does not provide sufficient written description for nucleotide sequences comprising at least 29 amino acids from SEQ ID NO:2, as claim 4 currently recites only nucleic acid molecules comprising a nucleotide sequence that encodes the amino acid sequence from amino acid number 33 to amino acid

number 141 of SEQ ID NO:2, which is clearly described in the specification (see, at least, Section 5.1), the present rejection of claim 4 under 35 U.S.C. § 112, first paragraph, has been overcome. Applicants therefore respectfully request that the rejection of claims 1 and 4 under 35 U.S.C. § 112, first paragraph, be withdrawn.

IX. Rejection of Claims 1, 2 and 4 Under 35 U.S.C. § 112, Second Paragraph

The Action next rejects claims 1, 2 and 4 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the invention.

The Action first rejects claim 1 as allegedly indefinite based on the term "at least 24 contiguous bases of nucleotide sequence first disclosed in the NHP polynucleotides described in SEQ ID NO:1". While Applicants submit that the term does not render the claim indefinite, this term has been replaced with "the nucleotide sequence of SEQ ID NO: 1". Applicants therefore request withdrawal of this rejection.

The Action next rejects claim 4 as allegedly indefinite because the specification "does not disclose the significance of amino acid 33 of SEQ ID NO:2. Applicants respectfully point out that the significance of amino acid 33 of SEQ ID NO:2 is disclosed at various points throughout the specification, most specifically at least at page 12, lines 8-11 ("The galanin-like consensus sequence begins at **amino acid number 33** of SEQ ID NOS:2 and 4 and this position will generally define the amino terminus of the mature form of the disclosed NHPs"; emphasis added). Applicants therefore request the withdrawal of this rejection.

The Action next rejects claim 1 as allegedly indefinite based on the term "NHP". While Applicants submit that the term does not render the claim indefinite, the term "NHP" has been removed from the claim. Applicants therefore request withdrawal of this rejection.

The Action rejects claim 2 as allegedly indefinite based on the term "stringent hybridization conditions", because the specific hybridization and washing conditions are not recited in the claim. Applicants stress that "a claim need not 'describe' the invention, such description being the role of the disclosure". *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986). However, while Applicants submit that the term is sufficiently definite, as a number of stringent hybridization conditions are defined in the specification and would be known to those of skill in the art,

solely in order to progress the case more rapidly toward allowance the claim has been revised to specifically recite "highly" stringent hybridization conditions. As the specification provides specific teaching regarding "highly stringent hybridization conditions", at least from page 3, line 32 through page 4, line 5, Applicants submit that revised claim 2 even more clearly meets the requirements of 35 U.S.C. § 112, second paragraph. Applicants therefore request withdrawal of this rejection.

X. Rejection of Claims 1 and 4 Under 35 U.S.C. § 102(b)

The Action next rejects claims 1 and 4 under 35 U.S.C. § 102(a), as allegedly anticipated by Zhao et al. (GenBank Accession Number AQ549952; "Zhao"). While Applicants do not necessarily agree with the present rejection, as claim 1 has been amended to recite the complete nucleotide sequence of SEQ ID NO:1, which is neither taught nor suggested by Zhao, and claim 4 has been amended to recite a nucleotide sequence that encodes the amino acid sequence from amino acid number 33 to amino acid number 141 of SEQ ID NO:2, which is neither taught nor suggested by Zhao, Applicants submit that the rejection of claims 1 and 4 under 35 U.S.C. § 102(a) has been overcome, and respectfully request withdrawal of the rejection.

XI. Conclusion

The present document is a full and complete response to the Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner Bunner have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,

July 1, 2002

Date

David W. Hibler Reg. No. 41,071
Agent for Applicants

LEXICON GENETICS INCORPORATED
(281) 863-3399